REMARKS

The Examiner has rejected Claims 2, 4-6 and 8 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which applicant regards as the invention. The amendments as stated hereinabove are deemed to overcome this rejection.

The Examiner has rejected Claims 1, 3, 5 and 7 under 35 U.S.C. 102(b) as being anticipated by JP 08-332087. Applicant respectfully traverses Examiner's rejection and requests reconsideration for the following reasons.

The JP 08-332087 patent used concentrated urea to help unfold the native chains in whole wool keratin and to expose their active groups. The workers then solublized wool keratin by reduction of -S-S- groups to -SH groups with mercaptoethanol, splitting native keratin to reduced alkali-soluble fractions. It is unlikely that this rough treatment allowed survival of any long-chain alpha-keratose, a relatively homogenous material, but instead reduced the wool to a soup of short chain amino acids containing reduced sulfur groups, which were then dried to a solid sheet. Laboratory chemists have long prized alcoholic KOH as a fine cleanser of laboratory glassware. In any case, the material discussed in JP 08-332087 was not conceived, intended, or used as a parenteral substance, but simply as an inert wettable scaffolding in which to embed an enzyme. Thus, the JP 08-332087 patent is therefore not germane to the use of alpha-keratose as a plasma expander, being neither conceived, patented, or described as such, or even of similar physical composition to alpha-keratose.

The Examiner has rejected Claims 1-8 under 35 U.S.C. 102(b) as being anticipated by Ewald *et al.* Applicant respectfully traverses Examiner's rejection and requests reconsideration for the following reasons.

Ewald *et al.* examines the usefulness of chicken feather keratin as a source material for a polypeptide plasma expander. Keratins are a widespread class of organized sulfur-containing proteins found in the animal kingdom with varying physical (filamentous, globular matrix, hard, soft, pleated sheets, scales) attributes, and chemical constituencies (high sulfur, low sulfur, and other amino acid constituents). Depending on starting material and method of solublization (*e.g.*, acid hydrolysis, enzymatic cleavage, reductive sulfitolysis, oxidative sulfitolysis) the soluble derivatives of keratin (keratose[s]) may contain mixtures of hard and soft keratins, high sulfur and low sulfur extracts, acid soluble and acid insoluble protein fractions, *i.e.*, materials with differing physical, chemical, and physiologic (toxic or antigenic) properties. Thus, mere use of the terms "keratose", (JP 08-332087) or "polypeptide solution of keratin" (Ewald) are too generic and lack the specificity required for application to a given use or process.

Ewald was attracted to chicken feather hydrolyzed keratin as a potential plasma expander because of its ready availability, a relatively large (50%) non-charged amino acid constituency, and lack of antigenicity. The Examiner states that "alpha-keratose would at least be one component of the solution disclosed by Ewald *et al.*", but that is not necessarily true since they never demonstrated the sulfur-bearing alpha-linked amino acid chains from

the complex mixture of oxidized (and undoubtedly cross-linked -S-O-S-) sulfonated (-SO3H) peptides in their soluble hydrolyzate, *i.e.,* a toxic brew.

The bulk (84%) of Ewald's complex hydrolyzate test material was acid soluble, typical of matrix gamma-keratose which the Applicant discards. Sulfur content of this fraction was negligible since only about 20% of amino acid residues of an overall already low 3.4% sulfur content were characteristic. Ewald's acid insoluble fraction, similarly complex, was not distinguishable chemically, electrophoretically, or physiologically from the acid soluble fraction. It, too, proved to be toxic upon intravenous infusion.

Results on toxicity and antigenicity (Table I and Figure 1 of Ewald) were obtained using only hydrolyzed whole feather keratin and not with a significantly distinct keratin fraction. Ewald did not isolate alpha-keratose in soluble form, but used whole sulfonated chicken feather keratin (probably with attendant oxygen bridges) in his intravenous trials. In Ewald's discussion of the "hemoclastic" reaction achieved by this material, Ewald points out a variety of causes for this effect, including "macromolecular substances" and "particulated matter" which might apply to his work. Just as iron must be extracted from its ore in order to be useful, so must alpha-keratose be extracted from its native source in order to be useful as a plasma expander.

It is therefore respectfully urged that a prima facie showing of anticipation or obviousness has not been made.

All grounds of objection and rejection having been overcome by the amendments hereinabove, reconsideration and a Notice of Allowance is respectfully requested.

Respectfully submitted,

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CERTIFICATE OF MAILING

I HEREBY CERTIFY that the foregoing was placed in an envelope and mailed via U.S. First Class Mail, postage prepaid to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on this the 21st day of November, 2003

The Commissioner is hereby authorized to charge any additional fees which may be required at any time during the prosecution of this application without specific authorization, or credit any overpayment, to Deposit Account No. 50-1667.

Harvey S. Kauget

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